UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,493	11/28/2001	Martin Handfield	01-662	1452

20306 7590 05/19/2004

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,493	HANDFIELD ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 17-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment

1. The amendment filed on 2/17/04 has been entered into the record.

Status of claims

2. Claims 15 and 28 have been amended.

Claims 15, 16 and 28 are under examination.

Claims 1-28 are pending in the application.

Claims 1-14 and 17-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected group.

Objection withdrawn

3. In view of amendment to claims, 15 and 28, the objection as they depend from non-elected claimed invention is withdrawn.

Claim Rejection - 35 USC § 112, first paragraph withdrawn

4. In view of the Declaration of record provided by Prof.Handfield 2/17/04, the rejection of claims 15-16 and 28 under 35 U.S.C. 112, first paragraph (total lack of enablement) is withdrawn.

Claim Rejections - 35 USC 102 maintained

5. The rejection of claim 28 under 35 U.S.C. 102(b) as being anticipated by Flemmig et al 1996(Clinical and Diagnostic Laboratory Immunology; 3, 678-681) is maintained as set forth in the previous office action.

Flemmig et al disclose an immunoblotting method for detecting the presence of A. actinomycetemcomitans antibody (see abstract and page 679, left column under SDS-PAGE and immunoblotting). The method comprises contacting membrane proteins from A. actinomycetemcomitans that were separated by gel-electrophoresis (SDS-PAGE) with sera from infected individuals and thus read on contacting a test sample with a polypeptide of the claimed invention. After washing, the strips were incubated with goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The presence of a band is considered positive because the antigen present on the strip bound to an antibody present in a test sample and forms an immunocomplex that is positively identified by goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The positive band indicates the presence of A. actinomycetemcomitans in a test sample (page 679, left column under SDS-PAGE and immunoblotting and figure 1). The disclosed outer membrane proteins inherently contain the claimed peptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 because the outer-membrane proteins were obtained from cell lysates that contain mixture of polypeptides including a peptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52. Therefore, the prior art anticipates the claimed invention. In the absence of evidence to the contrary the disclosed prior art reads on the claimed invention since the OMP proteins bind to the specific anti-OMP antibodies. Characteristics such as including 5 contiguous amino acids of SEQ.ID.NO: 52 would be inherent in the preparations of OMP proteins. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed on 2/17/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that Flemmig does not teach SEQ.ID.NO: 52 mainly because the proteins disclosed are outer membrane proteins that are isolated from the in vitro culture and the presently claimed proteins are obtained by IVIAT methodology. Further applicant states that the examiner's inherency may not be established by probabilities and possibilities and cites several case laws of record.

It is the position of the examiner that the claim 28 is drawn to a method of detecting the presence of A.actinomycetemcomitans (Aa) or A.actinimycetemcomitans antibody in a test sample and is rejected correctly over a method disclosed by Flemmig. Indeed the prior art method detected the presence of A.actinimycetemcomitans antibody by contacting outer membrane proteins from A. actinomycetemcomitans with a test sample. Applicant's attention is drawn to the language used in the claims "immunogenic polypeptide comprising at least five

contiguous amino acids of SEQ.ID.NO: 52". Applicant's use of the open-ended term "comprising " in the claims fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, outer membrane proteins read on the claimed immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52. Therefore, the disclosed method positively detects the presence of the antibodies and thus satisfies the purpose set forth in the preamble.
Applicant's argument that the protein used in the claimed method is obtained by IVIAT technology and therefore, the prior art method does not identify the antibody using outer membrane proteins in a sample is not correct because applicant failed to show outer membrane proteins do not contain the claimed immunogenic polypeptide. Applicant is arguing the limitation "IVIAT" technology" is not relevant as the proteins obtained by that technology are involved in the pathogenesis of the infection. Further, applicant is not claiming a method for detecting an antibody that specifically binds to the amino acid sequence SEQ.ID.NO: 52. Therefore, this rejection is maintained.

6. The rejection of claim 28 under 35 U.S.C. 102(b) as being anticipated by Ebersole et al 1995(J.Dent Res 74 (2) 658-666) is maintained as set forth in the previous office action.

Ebersole et al disclose an immunoblotting method for detecting the presence of A. actinomycetemcomitans antibody (see abstract and page 659, right column under Western immunoblotting). The method comprises contacting outer membrane proteins from A. actinomycetemcomitans that were separated by gel-electrophoresis (figure1)) with sera from infected individuals and thus read on contacting a test sample with a polypeptide of the claimed invention. After washing the strips were incubated with goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The presence of a band is considered positive because the antigen present on the strip bound to antibody present in a test sample and forms an immunocomplex, which is positively identified by goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The positive band indicates the presence of A. actinomycetemcomitans in a test sample (page 660, left column under SDS-PAGE and immunoblotting and figure 2). The disclosed outer membrane proteins (OMP) contain the claimed peptide comprising at least SEQ.ID.NO: 52 because the outer-membrane proteins were

obtained from cell lysates containing mixture of polypeptides including peptide comprising at least SEQ.ID.NO: 52. Therefore, the prior art anticipates the claimed invention. In the absence of evidence to the contrary the disclosed prior art reads on the claimed invention since the OMP proteins bind to the specific anti-OMP antibodies.

Applicants' arguments filed on 2/17/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that the art of record does not teach SEQ.ID.NO: 52 mainly because the proteins disclosed are outer membrane proteins that are isolated from the in vitro culture and the presently claimed proteins are obtained by IVIAT methodology.

The examiner rejected claim 28 , drawn to a method of detecting the presence of A.actinomycetemcomitans (Aa) or A.actinimycetemcomitans antibody in a test sample. Please note that the applicant is not claiming an antigen but claiming a method. Applicant's argument that the protein used in the claimed method is obtained by IVIAT technology and therefore, the prior art method does not identify the antibody using outer membrane proteins in a sample is not correct because the disclosed method detects the presence of A.actinimycetemcomitans antibody in a test sample as set forth in the claim. Applicant's attention is drawn to the language used in the claims "immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52". Applicant's use of the open-ended term "comprising " in the claims fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts and thus outer membrane proteins read on the immunogenic polypeptide. Further, applicant is not claiming a method for detecting an antibody that specifically binds to the amino acid sequence SEQ.ID.NO: 52 obtained by IVIAT technology. Therefore, this rejection is maintained.

7. The rejection of claims 15-16 under 35 U.S.C. 102(b) as being anticipated by Snyder et al 1991 EPO0439210 or EPO 0439211 or EPO0439212 is maintained as set forth in the previous office action.

Snyder et al 1991 EPO0439210, disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or antigen extract with polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen (see page 2, lines 1-5, 51 through page 3, lines 1-15). They form an immunocomplex and said complex was detected with a label such as alkaline phosphatase or peroxidase etc (see example 1, page 9, line 51 through page 11, line 34), said Aa antigen is expressed during infection (se page 1, lines 57-64) causing periodontal disease and therefore the method detects the presence of Aa or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipates the claimed invention.

Or

Snyder et al, EPO 0439211 disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or extract of an antigen with polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen (see page 8, column 13 through column 14, line 8) and forms an immunocomplex and said complex is detected with a label such as alkaline phosphatase or peroxidase etc (see page 8 column 14, line 9 through page 9, column16, line 27), said Aa antigen is expressed during infection (se page 1, lines 57-64) causing periodontal disease and therefore the method detects the presence of Aa (as low as 3000cells) or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipates the claimed invention.

Or

Snyder et al, EPO 0439212 disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or extract of an antigen with an polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen and forms an immunocomplex and said complex is detected with a label such as alkaline phosphatase or peroxidase etc (see page 13, column 21 and page 14, column 23 through column 24, lines 31), said Aa antigen is expressed during infection (se page 1, left column lines 5 through right column) causing periodontal disease and therefore the method detects the presence of Aa or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipates the claimed invention.

8. The rejection of claims 15-16 are under 35 U.S.C. 102(b) as being anticipated Snyder et al 1992, EPO 537830. is maintained as set forth in the previous office action.

Snyder et al 1992, disclose an ELISA method for detecting the presence of Aa or Aa antigen from different patients suffering from periodontal disease by contacting the antigen extract in a surfactant mixture with an antibody, specific to A.actinomycetemcomitans (see page 8, lines 17-45) in an ELISA plate. Immediately, peroxide/ antibody conjugate was added to the wells and sandwich complex formation was allowed for five minutes. After the last wash, the dye was added and the resulting signal was evaluated for the presence of Aa or Aa antigen in a test sample (see pages 8 - 9, lined 24-46 and Table 1, lines 5-15). The prior art anticipates the claimed invention.

Applicants' arguments filed on 2/17/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that Snyder et al do not teach or suggest the elements of the claimed invention because the antibodies used do not bind to a peptide comprising at least 5 amino acids of SEQ.ID.NO: 52. Applicant brings the examiner's attention to different parts of Snyder's polyclonal antibodies raised against bacteria and therefore, the antibodies are not specific to SEQ.ID.NO: 52. Further ,applicant states that the claimed protein , SEQ.ID.NO: 52 is obtained by IVIAT technology .

The examiner disagrees with the applicant because claims 15 and 16 are drawn to a method of detecting the presence of A.actinomycetemcomitans (Aa) or A.actinimycetemcomitans antigen in a test sample contacting with an antibody or a fragment thereof that specifically binds to a purified immunogenic polypeptide comprising at least 5 amino acids of SEQ.ID.NO: 52. Therefore, the examiner correctly rejected the claimed method using a method , which detects the presence of A.actinimycetemcomitans antigen in a test sample. Please note that the applicant is not a claiming a method for detecting the presence of A.actinimycetemcomitans IVIAT antigen as set forth in the SEQ.ID.NO: 52 . Applicant's argument that the protein used in the claimed method is obtained by IVIAT technology and antibodies to said antigen detects the presence of A.actinomycetemcomitans unlike the disclosed polyclonal antibody which has been used to detect antigen in a sample is not correct

because polyclonal antibodies have been shown to bind A.actinomycetemcomitans antigen as thus the method detects the presence of antigen in a sample. Therefore, this rejection is maintained.

New Claim Rejections - 35 USC 112, first paragraph based on the amendment

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "a method of detecting the presence of A.actinomycetemcomitans (Aa) or A.actinimycetemcomitans antigen (Aa antigen) in a test sample comprising: contacting a test sample with an antibody that specifically binds to a purified immunogenic polypeptide comprising the amino acid sequence set forth in SEQ.ID.NO: 52 ------ in a test sample" , does not reasonably provide enablement for method of detecting the presence of A.actinomycetemcomitans (Aa) or A.actinimycetemcomitans antigen (Aa antigen) in a test sample comprising: contacting a test sample with a fragment thereof that specifically binds to a purified immunogenic polypeptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 ----- in a test sample". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

10. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting the presence of A. actinomycetemcomitans antibody in a test sample comprising: contacting a test sample with purified immunogenic polypeptide comprising the amino acids of SEQ.ID.NO: 52, wherein the polypeptide specifically binds to A.actinimycetemcomitans antibody ---in a test sample" and does not reasonably provide enablement for a method of detecting the presence of A. actinomycetemcomitans antibody in a test sample comprising: contacting a test sample with purified immunogenic polypeptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 ----in a test sample." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In view of the Declaration of record provided by Prof.Handfield 2/17/04, the examiner has withdrawn the rejection for total lack of enablement because the declaration provided evidence that purified protein comprising SEQ.ID.NO: 52 has been used to identify antibody from patient's sera. However, neither the declaration nor the specification discloses fragments of antibody or fragments of SEQ.ID.NO: 52 have been used in a method. Therefore, the specification lacks support for a method of detecting the presence Aa antigen using fragments of antibody that specifically binds to at least 5 contiguous amino acids of SEQ.ID.NO: 52 in a test sample and a method of detecting the presence antibody using fragments of SEQ.ID.NO; 52 as claimed in claims 15, 16 and 28 respectively.

The specification does not support the broad scope of the claims encompassing fragments of antibody or fragments of SEQ.ID.NO: 52 (antigen) which can be predictably modified and which regions are critical; what variants, if any, can be made which retain the

biological activity of the intact protein; and the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. Further, Houghten et al. (Vaccines, 1986, Edited by Fred Brown: Cold Spring Harbor Laboratory) teach that changes/modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore affect antibody production (p. 21) as well as antibody binding. Houghten et al. also teach that "... combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection." And "a protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). Houghten et al. teach that point mutations at one key antigen residue could eliminate the ability of an antibody to recognize this altered antigen (p. 24).

Thus, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed methods using fragments of antibodies or antigens in a method for detecting the presence of A. actinomycetemcomitans antibody or antigen in a manner reasonably correlated with the scope of the claims broadly including any as presently claimed. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the protein renders activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins. However, even if it were shown that some modifications could be tolerated in the claimed peptide, for the reasons discussed the claims would still expectedly encompass significant changes, which could not be distinguished

without undue experimentation. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Remarks

11. Claims 15, 16 and 28 are rejected.

Conclusion

12. This application contains claims 1-14 and 17-27 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected group. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

14. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989.

The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

5/12/04

L. F. Smith

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600